Methylated nucleic acid sequences are also provided. For the first time, the present invention provides methylated chemical structures for the following genes: APOB, CACNA1G, CDX2, EGFR, FBN1, GPR37, HSPA6, IQGAP2, KL, PAR2, PITX2, PTCH, SDC1, and SDC4. One of skill in the art can now readily locate the CpG-rich sequences associated with these genes and identify such methylated forms of the genes/regulatory sequences by methods described herein (The gene sequences can be identified in a gene database found at the following uniform resource locator (url): ncbi.nim.nih.gov/UniGene/index.html). The invention provides CpG-rich regions from the above genes as set forth in SEQ ID Nos:105-119. Thus, in yet another embodiment, the invention provides an isolated nucleic acid molecule having at least one methylated Cytosine of a CpG dinucleotide in a CpG-rich region and encoding a gene selected from APOB, CACNA1G, CDX2, EGFR, FBN1, GPR37, HSPA6, IQGAP2, KL, PAR2, PITX2, PTCH, SDC1, and SDC4. The methylated C residue of a CpG dinucleotide is located within a CpG-rich region selected from SEQ ID NO:105-118 and SEQ ID NO:119.

C1

At page 35, please delete the paragraph at lines 38-40, and substitute therefor:

C2

Note: Y = C or T, R = G or A; row 1-SEQ ID NO:1 and 2; row 2-SEQ ID NO:3 and 4 and so forth through to SEQ ID NO:32, respectively. The gene sequences can be found in a gene database found at the following url address: ncbi.nim.nih.gov/UniGene/index.html.

At page 39, in the title of Table 5, please enter the following rewritten title:

Table 5 New genes differentially methylated in disease versus normal tissue

At page 67, please delete the paragraph at lines 13-25, and substitute therefor:

C3

Six g of total RNA, was reverse transcribed using the SUPERSCRIPT kit (GIBCO-BRL) for first strand cDNA synthesis. One hundred ng of cDNA was used as template for RT-PCR reactions. To design the RT-PCR primers, Blast search was performed using the rat CacnalG cDNA sequence (Genbank AF027984) reported previously (25) and exon-intron boundaries of the human CACNA1G were predicted by this analysis. Each primer set was designed to amplify the cDNA across several introns. Primer sequences and PCR conditions are available, at the following uniform resource locator (url): med.jhu.edu/methylation/primers. GAPDH was also amplified as a control using primers GAPDHF: 5'-CGGAGTCAACGGATTGGTCGTAT-3' (SEQ ID NO:55) and GAPDHR: 5'-AGCCTTCTCCATGGTGGTGAAGAC-3' (SEQ ID NO:56). All reactions were performed with RT(-) controls. PCR amplification was performed for 35 cycles of 95° C 30 sec, 60-65°C for 30 sec, 72°C for 30 sec, and the products were analyzed by agarose gel electrophoresis.

At page 68, please delete the first paragraph at lines 1-17, and substitute therefor:

C4

PCR reaction products were precipitated with ethanol, resuspended in diluted water and cloned into the pCR2.1 vector using the TA cloning kit (Invitrogen) according to the manufacturer's instruction. After transformation, plasmid DNA was purified using the Wizard Miniprep Kit (Promega). DNA sequence analysis was carried out at the Johns Hopkins University Sequence Facility using automated DNA sequencers (Applied Biosystems). Sequence homology was identified by the BLAST program of the National Center for Biological Information (NCBI) available at the following uniform resource locator (url):

C4

ncbi.nlm.nih.gov/BLAST/. An IMAGE cDNA clone (Genbank: H13333) was identified by BLAST analysis using the sequence of BAC AC004590 (Genbank) which includes MINT31. Putative genes (G1 and G2) were identified by GENSCAN (available at the following uniform resource locator (url): ccr-081.mit.edu/GENSCANMIT.html) using the BAC sequence data. IMAGE cDNA clone H1333) was then obtained from the American Type Culture Collection and completely sequenced. Potential transcription factor binding sites and promoter prediction were examined using the TBSS and TSSG programs respectively, available at the Baylor College of Medicine BCM Launcher the following uniform resource locator (url): kiwi.imgen.bcm.tmc.edu:8088/searchlauncher/launcher.html/). The nucleotide sequence of part of the 5' end of the cDNA of CACNA1G has been submitted to Genbank.

In the Claims

Please cancel claim 12 without prejudice.

Please enter the following rewritten claims: